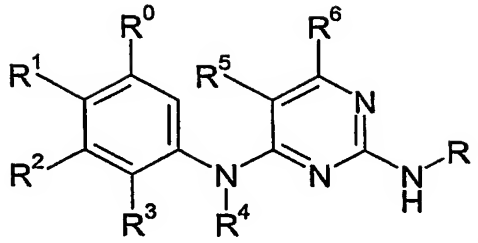
Claims

1. A compound of formula I



(I)

wherein

R is selected from C_{6-10}aryl, C_{5-10}heteroaryl, C_{3-12}cycloalkyl and C_{3-10}heterocycloalkyl;

each of R^0, R^1, R^2,and R^3 independently is hydrogen, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkinyl, C_3-C_8cycloalkyl, C_3-C_8cycloalkylC_1-C_8alkyl, C_5-C_{10}arylC_1-C_8alkyl, hydroxyC_1-C_8alkyl, C_1-C_8alkoxyC_1-C_8alkyl, aminoC_1-C_8alkyl, haloC_1-C_8alkyl, unsubstituted or substituted C_5-C_{10}aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1, 2 or 3 hetero atoms selected from N, O and S, hydroxy, C_1-C_8alkoxy, hydroxyC_1-C_8alkoxy, C_1-C_8alkoxyC_1-C_8alkoxy, haloC_1-C_8alkoxy, unsubstituted or substituted C_5-C_{10}arylC_1-C_8alkoxy, unsubstituted or substituted heterocyclyloxy, or unsubstituted or substituted heterocyclylC_1-C_8alkoxy, unsubstitued or substituted amino, C_1-C_8alkylthio, C_1-C_8alkylsulfinyl, C_1-C_8alkylsulfonyl, C_5-C_{10}arylsulfonyl, halogen, carboxy, C_1-C_8alkoxycarbonyl, unsubstitued or substituted carbamoyl, unsubstitued or substituted sulfamoyl, cyano, nitro, $-S(O)_{0-2}NR_{12}R_{13}$, $-S(O)_{0-2}R_{13}$, $-NR_{12}S(O)_{0-2}R_{13}$, $-C(O)NR_{12}R_{13}$, $-C(O)R_{13}$ and $-C(O)OR_{13}$; wherein R_{12} is selected from hydrogen and C_{1-6}alkyl; and R_{13} is selected from hydrogen, C_{1-6}alkyl and C_{3-12}cycloalkyl;

or R^0 and R^1, R^1 and R^2, and/or R^2 and R^3 form, together with the carbon atoms to which they are attached, a 5 or 6 membered carbocyclic or heterocyclic ring comprising 0, 1, 2 or 3 heteroatoms selected from N, O and S;

R^4 is hydrogen or C_1-C_8alkyl;

each of R^5 and R^6 independently is hydrogen, C_1-C_8alkyl, C_1-C_8alkoxyC_1-C_8alkyl, haloC_1-C_8alkyl, C_1-C_8alkoxy, halogen, carboxy, C_1-C_8alkoxycarbonyl, unsubstitued or substituted carbamoyl, cyano, or nitro;

R is unsubstituted or substituted by R_7, R_8, R_9, R_{10}, and R'_{10};

R_7, R_8, R_9, R_{10}, or R'_{10} is a substituent independently selected from hydrogen, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkinyl, C_3-C_8cycloalkyl, C_3-C_8cycloalkylC_1-C_8alkyl, C_5-C_{10}arylC_1-C_8alkyl, hydroxyC_1-C_8alkyl, C_1-C_8alkoxyC_1-C_8alkyl, aminoC_1-C_8alkyl, haloC_1-C_8alkyl, unsubstituted or substituted C_5-C_{10}aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1, 2 or 3 hetero atoms selected from N, O and S, hydroxy, C_1-C_8alkoxy, hydroxyC_1-C_8alkoxy, C_1-C_8alkoxyC_1-C_8alkoxy, haloC_1-C_8alkoxy, unsubstituted or substituted aminoC_1-C_8alkoxy, unsubstituted or substituted C_5-C_{10}arylC_1-C_8alkoxy, unsubstituted or substituted heterocyclyloxy, or unsubstituted or substituted heterocyclylC_1-C_8alkyl, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, unsubstitued or substituted amino, C_1-C_8alkylthio, C_1-C_8alkylsulfinyl, C_1-C_8alkylsulfonyl, C_5-C_{10}arylsulfonyl, heterocyclosulfonyl, halogen, carboxy, C_1-C_8alkylcarbonyl, C_1-C_8alkoxycarbonyl, unsubstitued or substituted carbamoyl, unsubstitued or substituted sulfamoyl, cyano, nitro, $-S(O)_{0-2}NR_{12}R_{13}$, $-S(O)_{0-2}R_{12}$, $-C(O)R_{11}$, $-OXR_{11}$, $-NR_{12}XR_{11}$, $-NR_{12}XNR_{12}R_{13}$, $-OXNR_{12}R_{13}$, $-OXOR_{12}$ and $-XR_{11}$;

or two adjacent substituents on R may form together with the carbon atoms to which they are attached, a unsubstitued or substituted 5 or 6 membered carbocyclic or heterocyclic ring comprising 0, 1, 2 or 3 heteroatoms selected from N, O and S;

X is a bond or C_{1-6}alkylene; and

R_{11} is independently selected from C_{6-10}aryl, C_{5-10}heteroaryl, C_{3-12}cycloalkyl and C_{3-10}heterocycloalkyl;

and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl of R_{11} is optionally substituted by 1 to 3 radicals independently selected from C_{1-6}alkyl, C_{3-10}heterocycloalkyl-C_{0-4}alkyl optionally substituted with C_{1-6}alkyl, $-C(O)R_{12}$, $-C(O)NR_{12}R_{13}$, $-XNR_{12}R_{13}$, $-NR_{12}XNR_{12}R_{13}$ and $-NR_{12}C(O)R_{13}$; wherein X is a bond or C_{1-6}alkylene; R_{12} and R_{13} are independently selected from hydrogen and C_{1-6}alkyl;

and salts thereof for the treatement of a disease associated to tyrosine kinase activity of anaplastic lymphoma kinase (ALK).

2. use of a compound of formula I according to claim 1 wherein

R^0 or R^2 independently is hydrogen, C_1-C_8alkyl, e.g. methyl, ethyl or isopropyl, hydroxyC_1-C_8alkyl, e.g. hydroxyethyl or hydroxybutyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, unsubstituted or substituted C_5-C_{10}aryl, e.g. phenyl or methoxyphenyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, e.g. morpholino, piperidino, piperazino or N-methylpiperazino, C_1-C_8alkoxy, e.g. methoxy, ethoxy or isopropoxy, haloC_1-C_8alkoxy, e.g. trifluoromethoxy, C_5-C_{10}aryloxy, e.g. phenoxy,

unsubstituted or substituted heterocyclyloxy, e.g. 1-methyl-4-piperidyloxy, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, e.g. 2-(1-imidazolyl)ethoxy, 3-morpholinopropoxy or 2-morpholinoethoxy, unsubstituted or substituted amino, e.g. methylamino, dimethylamino or acetylamino, C_1-C_8alkylsulfonyl, e.g. methylsulfonyl, halogen, e.g. fluoro or chloro, unsubstituted or substituted carbamoyl, e.g. cyclohexylcarbamoyl, piperidinocarbonyl, piperazinocarbonyl, N-methylpiperazinocarbonyl or morpholinocarbonyl, unsubstituted or substituted sulfamoyl, e.g. sulfamoyl, methylsulfamoyl or dimethylsulfamoyl; preferably hydrogen, piperazino, N-methylpiperazino or 1-methyl-4-piperidyloxy, $-S(O)_{0-2}NR_{12}R_{13}$, $-S(O)_{0-2}R_{13}$, $-NR_{12}S(O)_{0-2}R_{13}$, $-C(O)NR_{12}R_{13}$, and $-C(O)OR_{13}$ in particular hydrogen;

R^1 is hydrogen, C_1-C_8alkyl, e.g. methyl, ethyl or isopropyl, hydroxyC_1-C_8alkyl, e.g. hydroxyethyl or hydroxybutyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, unsubstituted or substituted C_5-C_{10}aryl, e.g. phenyl or methoxyphenyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, e.g. morpholino, piperidino, piperazino or N-methylpiperazino, C_1-C_8alkoxy, e.g. methoxy, ethoxy or isopropoxy, haloC_1-C_8alkoxy, e.g. trifluoromethoxy, C_5-C_{10}aryloxy, e.g. phenoxy, unsubstituted or substituted heterocyclyloxy, e.g. 1-methyl-4-piperidyloxy, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, e.g. 2-(1-imidazolyl)ethoxy, 3-morpholinopropoxy or 2-morpholinoethoxy, unsubstituted or substituted amino, e.g. methylamino, dimethylamino or acetylamino, C_1-C_8alkylsulfonyl, e.g. methylsulfonyl, halogen, e.g. fluoro or chloro, unsubstituted or substituted carbamoyl, e.g. cyclohexylcarbamoyl, piperidinocarbonyl, piperazinocarbonyl, N-methylpiperazinocarbonyl or morpholinocarbonyl, unsubstituted or substituted sulfamoyl, e.g. sulfamoyl, methylsulfamoyl or dimethylsulfamoyl; preferably hydrogen, piperazino, N-methylpiperazino, morpholino, 1-methyl-4-piperidinyloxy, 3-morpholinopropoxy or 2-morpholinoethoxy, in particular hydrogen;

R^3 is hydrogen, C_1-C_8alkyl, e.g. methyl or ethyl, hydroxyC_1-C_8alkyl, e.g. hydroxyethyl or hydroxybutyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 heteroatoms selected from N, O and S, e.g. 2-pyrrolidonyl or S,S-dioxoisothiazolidinyl, C_1-C_8alkoxy, e.g. methoxy, substituted amino, e.g. acetylamino, acetyl-methyl-amino, benzoylamino, methylsulfonylamino or phenylsulfonylamino, C_1-C_8alkylsulfonyl, e.g. methylsulfonyl, propyl-sulfonyl, cyclohexyl-sulfonyl, isopropyl-sulfonyl, C_5-C_{10}arylsulfonyl, e.g. phenylsulfonyl, halogen, e.g. fluoro or chloro, carboxy, substituted or unsubstituted carbamoyl, e.g. carbamoyl, methylcarbamoyl, ethyl-amino-carbonyl or dimethylcarbamoyl, unsubstituted or substituted sulfamoyl, e.g. sulfamoyl, methylsulfamoyl,

propylsulfamoyl, isopropylsulfamoyl, isobutylsulfamoyl, cyclopropylmethyl-sulfamoyl, 2,2,2-trifluoroethylsulfamoyl, dimethylsulfamoyl or morpholinosulfonyl dimethyl-sulfamoyl, ethyl-sulfamoyl, 1-ethyl-propyl-sulfamoyl, cyclopentyl-sulfamoyl, cyclobutyl-sulfamoyl; preferably sulfamoyl, methylsulfamoyl or propylsulfamoyl;

each pair of adjacent substituents R^0 and R^1, or R^1 and R^2, or R^2 and R^3 are $-CH_2-NH-CO-$, $-CH_2-CH_2-NH-CO-$, $-CH_2-CO-NH-$, $-CH_2-CH_2-CO-NH-$, $-CH_2-NH-SO_2-$, $-CH_2-CH_2-NH-SO_2-$, $-CH_2-SO_2-NH-$, $-CH_2-CH_2-SO_2-NH-$, $-CH_2-CH_2-SO_2-$, $-CH_2-CH_2-CH_2-SO_2-$, $-O-CH_2-O-$, or $-O-CF_2-O-$, and such pairs wherein hydrogen in NH is replaced by C_1-C_8alkyl; preferably the pair of adjacent substituents R^0 and R^1, or R^1 and R^2 being $-O-CH_2-O-$, and the pair of adjacent substituents R^2 and R^3 being $-CH_2-NH-CO-$ or $-CH_2-NH-SO_2-$.

R^4 is hydrogen or C_1-C_8alkyl, e.g. methyl; preferably hydrogen;

R^5 is hydrogen; C_1-C_8alkyl, e.g. methyl or ethyl, halogen, e.g. chloro or bromo, haloC_1-C_8alkyl, e.g. trifluoromethyl, cyano or nitro; preferably hydrogen, methyl, ethyl, chloro, bromo, trifluoromethyl or nitro; in particular chloro or bromo;

R^6 is hydrogen;

each of R^7 and R^9 independently is hydrogen, C_1-C_8alkyl, e.g. methyl, ethyl or isopropyl, hydroxyC_1-C_8alkyl, e.g. hydroxyethyl or hydroxybutyl, C_1-C_8alkylcarbonyl, e.g methyl carbonyl, aminoalkoxy, e.g diethylaminoethoxy, haloC_1-C_8alkyl, e.g. trifluoromethyl, unsubstituted or substituted C_5-C_{10}aryl, e.g. phenyl or methoxyphenyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, e.g. morpholino, piperidino, piperazino or N-methylpiperazino, C_1-C_8alkoxy, e.g. methoxy, ethoxy or isopropoxy, haloC_1-C_8alkoxy, e.g. trifluoromethoxy, C_5-C_{10}aryloxy, e.g. phenoxy, unsubstituted or substituted heterocyclyloxy, e.g. 1-methyl-4-piperidyloxy, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, e.g. 2-(1-imidazolyl)ethoxy, 3-morpholinopropoxy or 2-morpholinoethoxy, unsubstituted or substituted amino, e.g. methylamino, dimethylamino or acetylamino, C_1-C_8alkylsulfonyl, e.g. methylsulfonyl, heterocyclosulfonyl, e.g piperazinylsulfonyl, heterocyclocarbonyl, e.g. methylpirerazinylcarbonyl, cyano, halogen, e.g. fluoro or chloro, unsubstituted or substituted carbamoyl, e.g. cyclohexylcarbamoyl, piperidinocarbonyl, piperazinocarbonyl, N-methylpiperazinocarbonyl or morpholinocarbonyl, unsubstituted or substituted sulfamoyl, e.g. sulfamoyl, methylsulfamoyl or dimethylsulfamoyl; preferably hydrogen, methyl, isopropyl, trifluoromethyl, phenyl, methoxyphenyl, piperidino, piperazino, N-methylpiperazino, morpholino, methoxy, ethoxy, isopropoxy, phenoxy, 3-

morpholinopropoxy, 2-morpholinoethoxy, 2-(1-imidazolyl)ethoxy, dimethylamino, fluoro, morpholinocarbonyl, piperidinocarbonyl, piperazinocarbonyl or cyclohexylcarbamoyl;

R^8 is hydrogen, C_1-C_8alkyl, e.g. methyl, ethyl or isopropyl, hydroxyC_1-C_8alkyl, e.g. hydroxyethyl or hydroxybutyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, C_5-C_{10}aryl, e.g. phenyl or methoxyphenyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, e.g. morpholino, piperidino, piperazino or N-methylpiperazino, heterocyclylalkyl, e.g. methylpiperazinoethyl, heterocyclylcarbonyl, e.g. piperazinocarbonyl, heterocyclyl C_1-C_8alkylamino, e.g. pyridylethyl(methyl)amino, C_1-C_8alkoxy, e.g. methoxy, ethoxy or isopropoxy, haloC_1-C_8alkoxy, e.g. trifluoromethoxy, C_5-C_{10}aryloxy, e.g. phenoxy, unsubstituted or substituted heterocyclyloxy, e.g. 1-methyl-4-piperidyloxy, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, e.g. 2-(1-imidazolyl)ethoxy, 3-morpholinopropoxy or 2-morpholinoethoxy, unsubstituted or substituted amino, e.g. methylamino or dimethylamino, C_1-C_8alkylamino-C_1-C_8alkylamino, e.g. dimethylamino-propylamino, C_1-C_8alkylsulfonyl, e.g. methylsulfonyl, halogen, e.g. fluoro or chloro, unsubstituted or substituted carbamoyl, e.g. cyclohexylcarbamoyl, piperidinocarbonyl, piperazinocarbonyl, N-methylpiperazinocarbonyl or morpholinocarbonyl, unsubstituted or substituted sulfamoyl, e.g. sulfamoyl, methylsulfamoyl or dimethylsulfamoyl, cyano, or nitro; preferably hydrogen, methyl, piperidino, piperazino, N-methylpiperazino, morpholino, methoxy, ethoxy, trifluoromethoxy, phenoxy, 1-methyl-4-piperidyloxy, 3-morpholinopropoxy, 2-morpholinoethoxy, 3-(N-methylpiperazino)-propoxy, methylamino, fluoro, chloro, sulfamoyl or nitro;

R^{10} is hydrogen, C_1-C_8alkyl, e.g. methyl, ethyl or butyl, hydroxy, cyano, hydroxyC_1-C_8alkyl, e.g. hydroxyethyl or hydroxybutyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, C_1-C_8alkoxy, e.g. methoxy or ethoxy, cycloalkylalkoxy, aryloxy, haloC_1-C_8alkoxy, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, e.g. 2-(1-imidazolyl)ethoxy, unsubstituted or substituted amino, e.g. methylamino or dimethylamino, halogen, e.g. fluoro or chloro; carboxy, carbamoyl, or unsubstituted or substituted sulfamoyl, e.g. sulfamoyl, methylsulfamoyl or dimethylsulfamoyl; preferably methyl, butyl, methoxy, ethoxy, 2-(1-imidazolyl)ethoxy, methylamino, dimethylamino or fluoro; and

each pair of adjacent substituents R^7 and R^8, or R^8 and R^9 or R^9 and R^{10}, are –NH-CH=CH-, -CH=CH-NH-, –NH-N=CH-, –CH=N-NH-, -CH_2-CH_2-CH_2-, -CH_2-CH_2-CH_2-CH_2-, -CH_2-CH_2-O-, -$CH_2C(CH_3)_2$O-, -CH=$C(CH_3)$O-, -OCH_2CH_2O-, -(Morpholinopropyl)N-CH=CH-, -CH=CH-O-, -O-CH_2-O-, or -O-CF_2-O-; preferably the pair of adjacent substituents R^7 and R^8 or R^8

and R^9 being -O-CH_2-O- or the pair of adjacent substituents R^9 and R^{10} being -NH-CH=CH-, -CH=N-NH-, -CH_2-CH_2-CH_2-, -CH_2-CH_2-CH_2-CH_2- or -O-CF_2-O-.

3 use of a compound of formula I according to claim 1 or 2 wherein

R^7, R^8, R^9, R^{10} and R'^{10} are ethoxy, ethyl, propyl, methyl, t-butyl, trifluoromethyl, nitrile, cyclobutyloxy, 2,2,2-trifluoroethoxy, methoxy, isobutyloxy, t-butyloxy, isopropyloxy, methyl-amino-carbonyl, cyclopropyl-methoxy, dimethylamino-propyl-amino, methoxy-ethoxy, -XR_{11}, -$C(O)R_{11}$ and –OXR_{11}; wherein X is a bond, methylene or ethylene; R_{11} is selected from piperazinyl, piperidinyl, pyrrolidinyl, morpholino, azepanyl and 1,4-dioxa-8-aza-spiro[4.5]dec-8-yl; wherein R_{11} is optionally substituted by 1 to 3 radicals independently selected from methyl, isopropyl, acetyl, acetyl-methyl-amino, 3-dimethylamino-2,2-dimethyl-propylamino, ethyl-methyl-amino-ethoxy, diethyl-amino-ethoxy, amino-carbonyl, ethyl, 2-oxo-pyrrolidin-1-yl, pyrrolidinyl, pyrrolidinyl-methyl, piperidinyl optionally substituted with methyl or ethyl, morpholino, dimethylamino, dimethylamino-propyl-amino, methyl-amino and ethyl-amino.

4.use of a compound of formula I according to claim wherein

R^0 or R^2 independently is hydrogen, C_1-C_8alkyl, e.g. methyl, ethyl or isopropyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, e.g. morpholino, piperidino, piperazino or N-methylpiperazino, C_1-C_8alkoxy, e.g. methoxy, ethoxy or isopropoxy, unsubstituted or substituted heterocyclyloxy, e.g. 1-methyl-4-piperidyloxy, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, e.g. 2-(1-imidazolyl)ethoxy, 3-morpholinopropoxy or 2-morpholinoethoxy, unsubstituted or substituted amino, e.g. methylamino, dimethylamino or acetylamino, halogen, e.g. fluoro or chloro; preferably hydrogen, piperazino, N-methylpiperazino or 1-methyl-4-piperidyloxy, in particular hydrogen;

R^1 is hydrogen, C_1-C_8alkyl, e.g. methyl, ethyl or isopropyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, e.g. morpholino, piperidino, piperazino or N-methylpiperazino, C_1-C_8alkoxy, e.g. methoxy, ethoxy or isopropoxy, unsubstituted or substituted heterocyclyloxy, e.g. 1-methyl-4-piperidyloxy, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, e.g. 2-(1-imidazolyl)ethoxy, 3-morpholinopropoxy or 2-morpholinoethoxy, unsubstituted or substituted amino, e.g. methylamino, dimethylamino or acetylamino, halogen, e.g. fluoro or chloro; preferably hydrogen, piperazino, N-

methylpiperazino, morpholino, 1-methyl-4-piperidinyloxy, 3-morpholinopropoxy or 2-morpholinoethoxy, in particular hydrogen;

R^3 is hydrogen, C_1-C_8alkyl, e.g. methyl or ethyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 heteroatoms selected from N, O and S, e.g. 2-pyrrolidonyl or S,S-dioxoisothiazolidinyl, C_1-C_8alkoxy, e.g. methoxy, substituted amino, e.g. acetylamino, acetyl-methyl-amino, benzoylamino, methylsulfonylamino or phenylsulfonylamino, C_1-C_8alkylsulfonyl, e.g. methylsulfonyl, C_5-C_{10}arylsulfonyl, e.g. phenylsulfonyl, halogen, e.g. fluoro or chloro, carboxy, substituted or unsubstituted carbamoyl, e.g. carbamoyl, methylcarbamoyl or dimethylcarbamoyl, unsubstituted or substituted sulfamoyl, e.g. sulfamoyl, methylsulfamoyl, propylsulfamoyl, isopropylsulfamoyl, isobutylsulfamoyl, cyclopropylmethyl-sulfamoyl, 2,2,2-trifluoroethylsulfamoyl, dimethylsulfamoyl or morpholinosulfonyl; preferably sulfamoyl, methylsulfamoyl or propylsulfamoyl;

each pair of adjacent substituents R^0 and R^1, or R^1 and R^2, or R^2 and R^3 are -CH_2-NH-CO-, -CH_2-NH-SO_2-, -CH_2-CH_2-SO_2-, -O-CH_2-O-, or -O-CF_2-O-, and such pairs wherein hydrogen in NH is replaced by C_1-C_8alkyl; preferably the pair of adjacent substituents R^0 and R^1, or R^1 and R^2 being -O-CH_2-O-, and the pair of adjacent substituents R^2 and R^3 being -CH_2-NH-CO- or -CH_2-NH-SO_2-.

R^4 is hydrogen;

R^5 is hydrogen, halogen, e.g. chloro or bromo, haloC_1-C_8alkyl, e.g. trifluoromethyl, or nitro; preferably hydrogen, chloro, bromo, trifluoromethyl or nitro; in particular chloro or bromo;

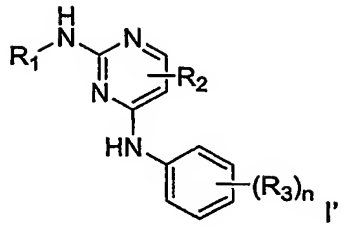
R^6 is hydrogen;

each of R^7 and R^9 independently is hydrogen, C_1-C_8alkyl, e.g. methyl, ethyl or isopropyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, unsubstituted or substituted C_5-C_{10}aryl, e.g. phenyl or methoxyphenyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, e.g. morpholino, piperidino, piperazino or N-methylpiperazino, C_1-C_8alkoxy, e.g. methoxy, ethoxy or isopropoxy, unsubstituted or substituted heterocyclyloxy, e.g. 1-methyl-4-piperidyloxy, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, e.g. 2-(1-imidazolyl)ethoxy, 3-morpholinopropoxy or 2-morpholinoethoxy, unsubstituted or substituted amino, e.g. methylamino, dimethylamino or acetylamino, halogen, e.g. fluoro or chloro, unsubstituted or substituted carbamoyl, e.g. cyclohexylcarbamoyl, piperidinocarbonyl, piperazinocarbonyl, N-methylpiperazinocarbonyl or morpholinocarbonyl, unsubstituted or substituted sulfamoyl, e.g. sulfamoyl, methylsulfamoyl or dimethylsulfamoyl; preferably hydrogen, methyl, isopropyl,

trifluoromethyl, phenyl, o-, m- or p-methoxyphenyl, piperidino, piperazino, N-methylpiperazino, morpholino, methoxy, ethoxy, isopropoxy, phenoxy, 3-morpholinopropoxy, 2-morpholinoethoxy, 2-(1-imidazolyl)ethoxy, dimethylamino, fluoro, morpholinocarbonyl, piperidinocarbonyl, piperazinocarbonyl or cyclohexylcarbamoyl;
R^8 is hydrogen, C_1-C_8alkyl, e.g. methyl, ethyl or isopropyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, C_5-C_{10}aryl, e.g. phenyl or methoxyphenyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, e.g. morpholino, piperidino, piperazino or N-methylpiperazino, C_1-C_8alkoxy, e.g. methoxy, ethoxy or isopropoxy, haloC_1-C_8alkoxy, e.g. trifluoromethoxy, C_5-C_{10}aryloxy, e.g. phenoxy, unsubstituted or substituted heterocyclyloxy, e.g. 1-methyl-4-piperidyloxy, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, e.g. 2-(1-imidazolyl)ethoxy, 3-morpholinopropoxy or 2-morpholinoethoxy, unsubstituted or substituted amino, e.g. methylamino or dimethylamino, halogen, e.g. fluoro or chloro, unsubstituted or substituted sulfamoyl, e.g. sulfamoyl, methylsulfamoyl or dimethylsulfamoyl, or nitro; preferably hydrogen, methyl, piperidino, piperazino, N-methylpiperazino, morpholino, methoxy, ethoxy, trifluoromethoxy, phenoxy, 1-methyl-4-piperidyloxy, 3-morpholinopropoxy, 2-morpholinoethoxy, 3-(N-methylpiperazino)-propoxy, methylamino, fluoro, chloro, sulfamoyl or nitro;
R^{10} is C_1-C_8alkyl, e.g. methyl, ethyl or butyl, haloC_1-C_8alkyl, e.g. trifluoromethyl, C_1-C_8alkoxy, e.g. methoxy or ethoxy, unsubstituted or substituted heterocyclylC_1-C_8alkoxy, e.g. 2-(1-imidazolyl)ethoxy, unsubstituted or substituted amino, e.g. methylamino or dimethylamino, halogen, e.g. fluoro or chloro; preferably methyl, butyl, methoxy, ethoxy, 2-(1-imidazolyl)ethoxy, methylamino, dimethylamino or fluoro; and
each pair of adjacent substituents R^7 and R^8, or R^8 and R^9 or R^9 and R^{10}, are –NH-CH=CH-, -CH=CH-NH-, –NH-N=CH-, –CH=N-NH-, -CH_2-CH_2-CH_2-, -CH_2-CH_2-CH_2-CH_2-, -O-CH_2-O-, or -O-CF_2-O-; preferably the pair of adjacent substituents R^7 and R^8 or R^8 and R^9 being -O-CH_2-O- or the pair of adjacent substituents R^9 and R^{10} being -NH-CH=CH-, -CH=N-NH-, -CH_2-CH_2-CH_2-, -CH_2-CH_2-CH_2-CH_2- or -O-CF_2-O-.

5. Use of a compound of formula I wherein the compound is selected from a compound of examples 1 to 53.

6. a compound of formula I' with the proviso that this does not include any of the compounds of examples 1 to 52 inclusive.



I'

in which:

n' is selected from 1, 2 and 3;

R'_1 is selected from C_{6-10}aryl, C_{5-10}heteroaryl, C_{3-12}cycloalkyl and C_{3-10}heterocycloalkyl;

wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl of R'_1 is optionally substituted by 1 to 3 radicals independently selected from C_{1-6}alkyl, C_{1-6}alkoxy, alkoxy-substituted-C_{1-6}alkyl, halo-substituted-C_{1-6}alkyl, halo-substituted-C_{1-6}alkoxy, -C(O)$NR'_5R'_6$, -$S(O)_{0-2}NR'_5R'_6$, -$S(O)_{0-2}R'_5$, -C(O)R'_4, -OXR'_4, -$NR'_5XNR'_5R'$, -O$XNR'_5R'_6$, -OXOR'_5 and –XR'_4;

wherein X' is a bond or C_{1-6}alkylene; R'_5 is selected from hydrogen and C_{1-6}alkyl; R'_6 is selected from hydrogen, C_{1-6}alkyl and C_{3-12}cycloalkyl-C_{1-4}alkyl; and R'_4 is independently selected from C_{6-10}aryl, C_{5-10}heteroaryl, C_{3-12}cycloalkyl and C_{3-10}heterocycloalkyl;

and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl of R'_4 is optionally substituted by 1 to 3 radicals independently selected from C_{1-6}alkyl, C_{3-10}heterocycloalkyl-C_{0-4}alkyl optionally substituted with C_{1-6}alkyl, -C(O)$NR'_5R'_6$, -$XNR'_5R'_6$, -$NR'_5XNR'_5R'_6$ and –$NR'_5C(O)R'_6$; wherein X is a bond or C_{1-6}alkylene; R'_5 and R'_6 are independently selected from hydrogen and C_{1-6}alkyl;

R'_2 is selected from hydrogen and halo, cyano, C_{1-6}alkyl, halo-substituted-C_{1-6}alkyl;

R'_3 is selected from halo, -$S(O)_{0-2}NR'_5R'_6$, -$S(O)_{0-2}R'_6$, -$NR'_5S(O)_{0-2}R'_6$, -C(O)$NR'_5R'_6$, –C(O)R'_6 and -C(O)OR'_6; wherein R'_5 is selected from hydrogen and C_{1-6}alkyl; and R'_6 is selected from hydrogen, C_{1-6}alkyl and C_{3-12}cycloalkyl;

and the pharmaceutically acceptable salts, hydrates, solvates, isomers and prodrugs thereof.

7. A compound of fomula I' according to claim 6 in which:

n' is selected from 1 and 2;

R'_1 is selected from C_{6-10}aryl and C_{5-10}heteroaryl; wherein any aryl or heteroaryl of R_1 is optionally substituted by 1 to 3 radicals independently selected from C_{1-6}alkyl, C_{1-6}alkoxy, -C(O)$NR'_5R'_6$, -$OX'R'_4$, -C(O)R'_4, -$NR'_5X'NR'_5R'_6$, -$OX'NR'_5R'_6$, -$OX'OR'_5$ and –$X'R'_4$; wherein X' is a bond or C_{1-6}alkylene; R'_5 is selected from hydrogen and C_{1-6}alkyl; R'_6 is selected from hydrogen, C_{1-6}alkyl and C_{3-12}cycloalkyl-C_{1-4}alkyl; and R'_4 is C_{3-10}heterocycloalkyl optionally substituted by 1 to 3 radicals independently selected from C_{1-6}alkyl, halo-substituted-C_{1-6}alkyl, C_{3-10}heterocycloalkyl-C_{0-4}alkyl optionally substituted with C_{1-6}alkyl, -C(O)$NR'_5R'_6$, -$X'NR'_5R'_6$, -$NR'_5X'NR'_5R'_6$ and –$NR'_5C(O)R'_6$; wherein X' is a bond or C_{1-6}alkylene; R'_5 and R'_6 are independently selected from hydrogen and C_{1-6}alkyl;

R'_2 is selected from hydrogen and halo;

R'_3 is selected from halo, -$S(O)_{0-2}NR'_5R'_6$, -$S(O)_{0-2}R'_6$, -$NR'_5S(O)_{0-2}R'_6$, -C(O)$NR'_5R'_6$ and -C(O)OR'_6; wherein R'_5 is selected from hydrogen and C_{1-6}alkyl; and R'_6 is selected from hydrogen, C_{1-6}alkyl and C_{3-12}cycloalkyl.

8. A compound of formula I' according to claim 6 or 7 in which R'_1 is selected from phenyl, pyridinyl, pyrazolyl and pyrimidinyl; wherein any aryl or heteroaryl of R'_1 is optionally substituted by 1 to 3 radicals independently selected from ethoxy, ethyl, propyl, methyl, t-butyl, trifluoromethyl, nitrile, cyclobutyloxy, 2,2,2-trifluoroethoxy, methoxy, isobutyloxy, t-butyloxy, isopropyloxy, methyl-amino-carbonyl; cyclopropyl-methoxy, dimethylamino-propyl-amino, methoxy-ethoxy, -$X'R'_4$, -C(O)R'_4 and –$OX'R'_4$; wherein X' is a bond, methylene or ethylene; R'_4 is selected from piperazinyl, piperidinyl, pyrrolidinyl, morpholino, azepanyl and 1,4-dioxa-8-aza-spiro[4.5]dec-8-yl; wherein R'_4 is optionally substituted by 1 to 3 radicals independently selected from methyl, isopropyl, acetyl, acetyl-methyl-amino, 3-dimethylamino-2,2-dimethyl-propylamino, ethyl-methyl-amino-ethoxy, diethyl-amino-ethoxy, amino-carbonyl, ethyl, 2-oxo-pyrrolidin-1-yl, pyrrolidinyl, pyrrolidinyl-methyl, piperidinyl optionally substituted with methyl or ethyl, morpholino, dimethylamino, dimethylamino-propyl-amino, methyl-amino and ethyl-amino.

9. A compound of of formula I' according to claim 6, 7 or 8 in which R'_2 is selected from hydrogen and halo; and R'_3 is selected from halo, dimethyl-sulfamoyl, isobutyl-sulfamoyl, methyl-sulfamoyl, ethyl-sulfamoyl, propyl-sulfonyl, ethyl-amino-carbonyl, 1-ethyl-propyl-

sulfamoyl, cyclopentyl-sulfamoyl, isopropyl-sulfamoyl, cyclohexyl-sulfonyl, cyclopropyl-methyl-sulfamoyl, cyclobutyl-sulfamoyl, isopropyl-sulfonyl,

10. A compound of formula I according to any one of claim 6 to 9 wherein the compound is a compound of example 53.

11. A pharmaceutical composition comprising a compound according to any one of claims 1 to 9, as active ingredient together with one or more pharmaceutically acceptable diluents or carriers.

12. The use of a compound according to any one of claims 1 to 9 for the manufacture of a medicament for the treatment or prevention of neoplastic diseases and immune system disorders.

13. A combination comprising a therapeutically effective amount a compound according to any one of claims 1 to 9 and one or more further drug substances, said further drug substance being useful in the treatment of neoplastic diseases or immune system disorders.

14. A method for the treatment of neoplastic diseases and immune system disorders in a subject in need thereof which comprises administering an effective amount of a compound according to any one of claims 1 to 9 or a pharmaceutical composition comprising same.

15. Use of a compound according to any one of claims 1 to 9 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of a disease which responds to inhibition of FAK and/or ALK and/or ZAP-70 and/or IGF–IR.

16. The use according to claim 15, wherein the disease to be treated is selected from proliferative disease .

17. The use according to claim 16, wherein the proliferative disease to be treated is selected from a tumor of, breast, renal , prostate, colorectal, thyroid, ovarian, pancreas, neuronal, lung, uterine and gastro-intestinal tumours as well as osteosarcomas and melanomas.

18. The use according to claim 15, wherein the disease to be treated is an immune disease.

19. Use of a compound according to any one of claims 1 to 9 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of inflammatory and/or an immune disorder.

20. Use according to claim 19 wherein the inflammatory and/or immune disorder is selected from transplant rejection, allergy and autoimmune disorders mediated by immune cells including T lymphocytes, B lymphocytes, macrophages, dendritic cells, mast cells and eosinophils.

21. The use according to any one of claims 14 to 19, wherein the compound is 2-[5-Bromo-2-(2-methoxy-5-morpholin-4-yl-phenylamino)-pyrimidin-4-ylamino]-N-methyl-benzenesulfonamide or5-Chloro-N*2*-{2-methoxy-4-[4-(4-methyl-piperazin-1-yl)-piperidin-1-yl]-phenyl}-N*4*-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2,4-diamine or a pharmaceutically acceptable salt thereof.

22. The use according to any one of claims 14 to 19, wherein the compound is selected from 2-[5-chloro-2-(2-methoxy-4-morpholin-4-yl-phenylamino)-pyrimidin-4-ylamino]-N-methyl-benzamide, N^2-(4-[1,4']Bipiperidinyl-1'-yl-2-methoxy-phenyl)-5-chloro-N^4-[2-(propane-1-sulfonyl)-phenyl]-pyrimidine-2,4-diamine and 2-{5-Chloro-2-[2-methoxy-4-(4-methyl-piperazin-1-yl)-phenylamino]-pyrimidin-4-ylamino}-N-isopropyl-benzenesulfonamide, or 5-Chloro-N*2*-{2-methoxy-4-[4-(4-methyl-piperazin-1-yl)-piperidin-1-yl]-phenyl}-N*4*-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2,4-diamine a pharmaceutically acceptable salt thereof.